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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,692	12/27/2001	Peter Gill	7500.331USC1	2411
23552	7590	06/29/2004	EXAMINER	
MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903			SPIEGLER, ALEXANDER H	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

847

Office Action Summary

Application No.

10/034,692

Applicant(s)

GILL ET AL.

Examiner

Alexander H. Spiegler

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 December 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/624,627.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/27/01 & 9/6/02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 1-45) in the reply filed on March 29, 2004 is acknowledged.

Applicants' argue "the basis for Applicants' traversal is that the Examiner has not shown how searching both groups of claims would be unduly burdensome". See Applicants' response on page 1.

Applicants' argument has been considered, but is not persuasive. For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the instant case, the serious burden of search has been established by, at least, the different classification of the inventions. See page 2 of the Office Action mailed on September 29, 2003. Accordingly, the restriction requirement is maintained.

Status of the Application

2. Currently, claims 1-46 are pending, Claims 1-45 are rejected herein and Claim 46 has been withdrawn from consideration. See 37 CFR 1.142(b) and MPEP § 821.

Information Disclosure Statement

3. The information disclosure statements of December 27, 2001 and September 6, 2002 comply with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see signed PTO-1449s).

Sequence Notes

4. The Sequence Listing filed in this application complies with the requirements of 37 CFR 1.821-1.825 and has been entered.

Specification

5. The disclosure is objected to because of the following informalities:

A) The abstract of the disclosure contains two paragraphs. Applicant is reminded of the proper format for an abstract of the disclosure is generally limited to a single paragraph. See MPEP 608.01(b)

B) In the Brief Descriptions of the Drawings, there is not an adequate description of Figures 1a-e, 3a-3e, 8a-8f, 9a-9d, 10a-10e, 12a-12e, 13a-13b. Applicants' should provide a separate description for each Figure, e.g., a description for Figure 1a, 1b, 1c, etc.

C) Some of the drawings have nucleic acid sequences (e.g., 7, 11, 21, 25, etc.), but do not contain the appropriate SEQ ID NOS for these sequences.

D) Claim 18 recites "in which the distinctive unit is a dye, dye label...emitter of radiation, characteristic isotope", which could be amended to recite "wherein the distinctive unit is selected from the group consisting of a dye, dye label...emitter of radiation, and characteristic isotope".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. Claims 1-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-45 are indefinite over the recitation of “the DNA”, because it is not clear as to whether of not “the DNA” refers the amplified product (i.e. first amplified product) or the DNA from the sample.

B) Claims 1-45 are indefinite over the recitation of “examining one or more characteristics” because it is not clear as to what is encompassed by “characteristics of the further amplified product”. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

C) Claims 1-45 are indefinite over the recitation “one side of the SNP under investigation” it is not clear as to what is encompassed by “one side of the SNP under investigation”. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

D) Claims 1-45 are indefinite because claim 1 is drawn to a method for investigating single nucleotide polymorphisms, however, the final step is for examining one or more characteristics of the further amplified product. The claims do not set forth the relationship between examining one or more characteristics of the further amplified product and a method for investigating single nucleotide polymorphisms. Therefore, it is not clear as to whether the claims are intended to be limited to a method of investigating single nucleotide polymorphisms or a method for examining one or more characteristics of the further amplified product.

E) Claims 1-45 are indefinite over the recitation of “the SNP” because this recitation lacks antecedent basis.

F) Claim 2 is indefinite over the recitation “the primers” because this recitation lacks antecedent basis (i.e. it is not clear as to whether this recitation is referring to the first or second set of primers).

G) Claim 2 is indefinite over the recitation “provided with an SNP identifying portion” because it is not clear as to what a “SNP identifying portion” is and how a primer is “provided” with one. The claim also recites, “SNP identity portion” and it is not clear as to whether this is the same as the “SNP identifying portion” or some other portion. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

H) Claim 2 is indefinite over the recitation of “the primer with an SNP identity portion” because this recitation lacks antecedent basis, since “primer with an SNP identity portion” is not previously recited.

I) Claim 3 is indefinite over the recitation “provided with a sequence equivalent” because it is not clear as to what is encompassed by a “sequence equivalent to the sequence of the further portion” and how a further portion is “provided” with one. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

J) Claim 4 is indefinite over the recitation of “which matches the sequence of the locus sequence in the vicinity of the SNP under investigation...” because it is not clear as to what “matching sequences” are, what constitutes the “vicinity of the SNP under investigation”, and it is not clear as to what “the locus commencing at between one and ten bases to the respective sides of the SNP” is. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

K) Claim 5 is indefinite over the recitation of “for each possible identity of the SNP” because it is not clear as to what is meant by this recitation, and specifically, it not clear as to what a “possible identity of a SNP” encompasses. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

L) Claims 6-7 are indefinite over the recitation “the further portion...by SNP related portion” because it is not clear as to what is meant by this recitation. It is not clear as to what primer is being referred to, and what a “SNP related portion” is and how it attaches portions of primers. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

M) Claims 7 and 12 are indefinite over the recitation of “SNP identifying portion” because this recitation lacks antecedent basis.

O) Claim 7 is indefinite over the recitation of “have equivalent identity” because it is not clear what is meant by this recitation and it is not defined in the specification. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

P) Claim 8 is indefinite over the recitation of “a set” because it is not clear as to whether or not this is referring to the first set of primers or some other set of primers.

Q) Claim 8 is indefinite over the recitation of “provided with identical sequences in each primer” because it is not clear as to whether the primers in the set are identical or the region containing the locus specific portion is identical for all the primers.

R) Claims 9-10 are indefinite over the recitation of “match” and “sequence matching” because it is not clear as to what is meant by these recitations or how one “matches” sequences.

Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

S) Claims 9-10 are indefinite over the recitation of “the locus sequence” because this recitation lacks antecedent basis.

T) Claims 10 and 14 are indefinite because it is not clear as to how the sequence of the further portion does not anneal to a sequence of “any published part of the entire DNA sequence of homo sapiens”. Any sequence that is complementary to the sequence of the further portion will anneal to the sequence of the further portion. It is not clear as to how this claim further limits Claim 1; especially considering the claim does not recite any limitations of the sequence of the further portion and the fact that millions of parts of the entire DNA sequence from homo sapiens have been provided in published literature.

U) Claim 11 is indefinite over the recitation of “for each potential identity of the SNP” because it is not clear as to what is meant by this recitation. It is not clear as to what an “a potential identity of a SNP” encompasses.

V) Claim 12 is indefinite over the recitation of “SNP repeat identifying portion” because it is not clear as to what is meant by this recitation and it is not defined in the specification. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

W) Claim 13 is indefinite over the recitation of “a sequence which pairs...in the vicinity of the SNP” because it is not clear as to how sequences “pair” and what “the vicinity of the SNP identifying portion and/or SNP repeat related portion” constitutes. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

X) Claim 14 is indefinite over the recitation of “further second portion” because this recitation lacks antecedent basis.

Y) Claim 15 is indefinite over the recitation of “the SNP repeat identifying portions and/or second SNP identifying portion” because this recitation lacks antecedent basis.

Z) Claim 16 is indefinite over the recitation of “the amplification products resulting being of different lengths” because it is not clear what amplification products of different lengths are being referred too.

AA) Claims 17-20, 38-40, and 45 are indefinite over the recitation of “a distinctive unit” because it is not clear as to what a “distinctive unit” constitutes and this recitation is not defined in the specification.

AB) Claims 17-20 are indefinite because it is not clear as to how “one or more characteristics of the further amplified products are investigated by means of the presence and/or absence of a distinctive unit”. (e.g., it is not clear as to whether a single nucleotide polymorphism will be detected by a label or some other method of detection) Furthermore, it is not clear how the presence and absence of the distinctive unit are possible.

AC) Claim 18 is indefinite over the recitation of “characteristic isotope” because it is not clear what is meant by this recitation and this recitation is not defined in the specification. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AD) Claim 19 is indefinite over the recitation of “second set” because it lacks antecedent basis. Applicant can overcome this rejection by amending the claim to recite “second set of primers”.

AE) Claim 20 is indefinite over the recitation of “the distinctive unit is indicative of the nucleotide presence of the SNP” because it is not clear how the presence and/or absence of the distinctive unit “is indicative of the nucleotide presence of the SNP. Furthermore, it is not clear what “the nucleotide presence” of the SNP is. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AF) Claims 21, 25, and 42 are indefinite over the recitation of “of at least in part” because it is not clear as what is encompassed by this recitation.

AG) Claim 22 is indefinite over the recitation of “are different from one another with respect to at least 25% of the nucleotides forming the further portion of the forward primers” because it is not clear how to determine when forward primers “are different from one another with respect to at least 25% of the nucleotides forming the further portion of the forward primers”.

AH) Claim 23 is indefinite over the recitation of “the distinguishing portion” because this recitation lacks antecedent basis.

AI) Claim 23 is indefinite over the recitation of “intermediate location with the sequence of the further portion” because it is not clear as to what is meant by this recitation. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AJ) Claim 24 is indefinite over the recitation of “provided with one or more portions which correspond” because it is clear as to what is “provided”, how they are “provided”, or how the one or more portions “correspond” with one or more portions.

AK) Claim 25 is indefinite over the recitation of “are equivalent...outside the distinguishing portion of the further portion” because it is not clear as to what “equivalent”

nucleotides are. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AL) Claims 28-29 are indefinite over the recitation of “at least some of the cycles of the amplification process is such that at least 80% of the second set of primers remain single stranded” because it is not clear as to how many cycles are being referred to (i.e. all but one, one, two, etc.), and it is unclear as how one determines when at least 80% of the second set of primers remain single stranded.

AM) Claim 30 is indefinite because claim 1, does not refer to “cycles”, and it is not clear how the “annealing temperature” is related to claim 1.

AN) Claims 31-32 are indefinite over the recitation of “the annealing temperature” and “the amplification process” because these recitations lack antecedent basis.

AO) Claim 33 is indefinite because it is not clear whether the amplification products and the second set of primers are separated or one or more second sets of primers are separated.

AP) Claims 34-36 are indefinite over the recitation of “having a sequence which anneals with at least part of the sequence of one of the further amplified products” because it is not clear as to what “at least part of the sequence” refers to (e.g., the whole sequence, 1 nucleotide, etc.). Furthermore, it is not clear as to what is encompassed by “components retained on a solid support”.

AQ) Claim 35 is indefinite over the recitation of “the base before the base which is the SNP side” because it is not clear as to what the SNP side is, and where “the base before the base which is the SNP side” is located.

AR) Claim 36 is indefinite over the recitation of “anneals to the further amplified product along the sequence corresponding...” because it is not clear as to what “along the sequence corresponding” means. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AS) Claim 38 is indefinite over the recitation of “further components to introduce a distinctive unit” because it is not clear as to what “further components” are and how they introduce a “distinctive unit”. Furthermore, it is not clear as to what a distinctive unit is. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

AT) Claim 40 is indefinite over the recitation of “the end base” because this recitation lacks antecedent basis.

AU) Claim 45 is indefinite over the recitation of “a distinctive unit relative to each other” because it is not clear as to what is meant by this recitation. Furthermore, this recitation is not defined in the specification, nor is this recitation an art-recognized term.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-16 and 21-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Parnavitana (Molecular and Cellular Probes (1998) 12: 309-315).

Due to the ambiguity of the claims (see above), the claims have been broadly interpreted as comprising a nested PCR reaction.

Paranavitana teaches a non-radioactive detection of *K-ras* mutations by nested allele specific PCR and oligonucleotide hybridization. Specifically, Paranavitana teaches a method of detecting point mutations (i.e. single nucleotide polymorphisms) in a DNA sample comprising, contacting a DNA sample with a first set of primers (wherein the first set of primers comprises a locus specific portion (i.e. allele specific primer, Primer A) and a further portion (i.e. codon 12 second position common primer, B), amplifying the DNA to give an amplification product, contacting at least a portion of the amplified product with at least one second set of primers, amplifying the DNA using the second set of primers to give a further amplified product, and examining the presence or absence of the *K-ras* point mutations (pg. 310 and 311). The reference teaches that the point mutations observed in the nested allele specific PCR were confirmed by using a non-radioactive detection method of dot blot hybridization (i.e., PCR products are attached to a solid support and 3' labelled with Digoxigenin-11 ddUTP oligonucleotide probes are hybridized to the PCR products) (pg. 311-312).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parnavitana (Molecular and Cellular Probes (1998) 12: 309-315), as applied to Claims 1-16 and 21-45 above, and in view of Wu et al. (PNAS (1989) 86: 2757-2760).

The teachings of Parnavitana are presented above. Specifically, Parnavitana teaches a method of detecting point mutations (i.e. single nucleotide polymorphisms) in a DNA sample comprising, contacting a DNA sample with a first set of primers (wherein the first set of primers comprises a locus specific portion (i.e. allele specific primer, Primer A) and a further portion (i.e. codon 12 second position common primer, B), amplifying the DNA to give an amplification product, contacting at least a portion of the amplified product with at least one second set of primers, amplifying the DNA using the second set of primers to give a further amplified product, and examining the presence or absence of the *K-ras* point mutations (pg. 310 and 311). Parnavitana does not teach the investigation of a single nucleotide polymorphism by means of the presence or absence of a distinctive unit in the further amplified product.

Wu teaches the allele-specific enzymatic amplification of β -globin genomic DNA from diagnosis of sickle cell anemia. Specifically, Wu teaches performing allele specific PCR (i.e. using one specific primer for the sickle cell allele and one primer specific from the normal allele) for detecting a polymorphism between the normal and sickle cell β -globin gene (see abstract and pgs. 2757-58). Wu teaches that this method could be improved (i.e. by eliminating the gel separation step) by differentially labeling the PCR primers (i.e. with biotin or fluorescence), and thereby labeling the PCR product (pg. 2758). Specifically, Figure 3, shows a dual labeling system suitable for allele-specific PCR, wherein one of the primers is labeled at its 5' end with a

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fluorescent group (pg. 2759). Therefore, Wu teaches that the labeling of the 5' forward primer can be used to improve the method of detecting polymorphisms through allele-specific PCR.

Accordingly, in view of the teachings of Wu, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Parnavitana so as to have investigated a SNP by means of the presence or absence of a distinctive unit in the further amplified product, by labeling a primer used in the amplification reaction with fluorescence, for example. One of ordinary skill in the art would have been motivated to modify the method of Parnavitana to have investigated a SNP by means of the presence or absence of a distinctive unit in the further amplified product in order to have achieved the benefits taught by Wu of providing a more efficient means of detecting SNPs by eliminating the gel separation step.

Conclusion

11. No Claims are allowable.

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Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

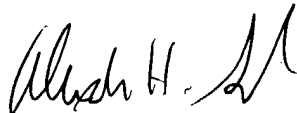
If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

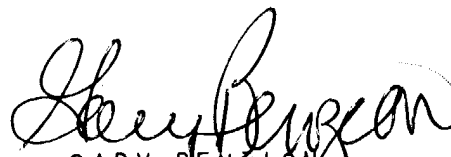
Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.


Alexander H. Spiegler
June 23, 2004


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6/22/2004